

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: J. Varner
Serial No.: 10/573,944 Group No.: 1644
Filed: 04/23/2007 Examiner: Michail A. Belyavskyi
Entitled: **METHODS FOR ALTERING HEMATOPOIETIC PROGENITOR
CELL ADHESION, DIFFERENTIATION, AND MIGRATION**

**DECLARATION UNDER 37 C.F.R. §1.132
BY DR. DAVID CHERISH**

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Commissioner for Patents
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Examiner Belyavskyi:

1. I, Dr. David Cheresh, am the subject of the attached *Curriculum Vitae* and author of the publications shown on the list attached thereto. I am Vice Chair for Research, Department of Pathology, UCSD, La Jolla, CA. I am also Professor, Department of Pathology, Moores UCSD Cancer Center, La Jolla, CA, and Director for Translational Research, Moores UCSD Cancer Center. I am married to the inventor, Dr. Judith Varner.

2. I have read and understand the above-identified patent application, and pending claims.

3. I have read and understand Papayannopoulou *et al.* (WO 94/11027).

4. **The claimed invention's target tissue is different from that in Papayannopoulou *et al.***

Papayannopoulou's methods require administering, to **bone marrow tissue**, agents that alter integrin $\alpha 4 \beta 1$'s binding to its ligand. In contrast, the invention's methods exclude bone

marrow endothelial tissue by reciting that the target tissue is “**not bone marrow**” endothelial tissue.

In particular, Papayannopoulou *et al.* discloses methods only for altering integrin $\alpha 4 \beta 1$'s binding to its ligand in **bone marrow**, which is distinguished from the instantly recited “**not bone marrow** endothelial tissue.” In particular, Papayannopoulou *et al.*'s methods relate to administering a blocking agent of integrin $\alpha 4 \beta 1$ to hematopoietic stem cells in bone marrow, thereby effecting their release (*i.e.*, peripheralization) from bone marrow into peripheral blood. In this regard, Papayannopoulou *et al.* explains that

“Applicant believes that administering a blocking agent of VLA-4 antigens on the surface of hematopoietic stem cells and CD34+ cells causes peripheralization of these cells by mediating **release** of the cells from the **marrow** environment via disruption of interactions between VLA-4 and its microenvironmental ligands, such as fibronectin and/or VCAM-1 on stromal cells or in the ECM.”¹

Thus, Papayannopoulou *et al.*'s methods relate to a different tissue (*i.e.*, **bone marrow**) from the instantly recited tissue that is “**not bone marrow** endothelial tissue.”

5. **The claimed invention's “adhesion” and Papayannopoulou *et al.* “peripheralization” are different phenomena**

Based on my understanding of the teachings of the instant Specification, of the prior art, and of Papayannopoulou *et al.*, it is my opinion that Papayannopoulou *et al.* does not disclose the claims' step c) since Papayannopoulou discloses “peripheralization,” which is a different phenomenon from the claimed invention's “adhesion.” This is explained further below.

A. **The meaning of the claimed invention's “adhesion” is understood from the teachings of the Specification and the prior art cited therein**

Pending Claim 1 recites “**adhesion**” between two cell types.

¹ (Emphasis added) Papayannopoulou *et al.*, page 25, lines 1-9.

The instant Specification refers to the teachings of several prior art references in connection with cell-to-cell “**adhesion**” as follows”

“Integrin $\alpha 4 \beta 1$ interactions with fibronectin and/or VCAM are also involved in . . . **adhesion** of immune cell precursors to bone marrow EC and for the homing of these cells back to the bone marrow (Simmons (1992) Blood. 80, 388-395; Papayannopoulou (2001) Blood 98, 2403-2411; Craddock (1997) Blood 90, 4779-4788; and Miyake (1991) J. Cell Biol. 114, 557-565).” Specification, page 23, lines 29-36.

“In fact, integrin $\alpha 4 \beta 1$ -VCAM interactions play obligatory roles in facilitating heterotypic cell **adhesion** *in vivo* during embryonic development, (chorion-allantois, endocardium-myocardium, primary myoblast fusions), in immune cell trafficking (extravasation of lymphocytes, monocytes, and eosinophils in inflammation) and in retention of immune cell precursors in the bone marrow (Rosen , Cell. 1992 Jun 26;69(7):1107-19).” Specification, page 68, lines 28-33.

“. . . hematopoietic precursor cells use $\alpha 4 \beta 1$ to **adhere** to bone marrow endothelium (Simmons (1992) Blood. 80, 388-395; Papayannopoulou (2001) Blood 98, 2403-2411; Craddock (1997) Blood 90, 4779-4788; Miyake (1991) J. Cell Biol. 114, 557-565).” Specification, page 73, lines 25-28.

From the above teachings of the Specification, and the prior art cited therein, it is my understanding that the claimed invention’s “**adhesion**” refers to the **binding** of an extracellular domain of a membrane protein on one cell type with a second molecule that is on the surface of another cell type.

B. The meaning of Papayannopoulou *et al.*’s “peripheralization”

Papayannopoulou *et al.* discloses that

“peripheralization of hematopoietic stem cells” means “**increasing the number** of hematopoietic stem cells and CD34⁺ cells in peripheral blood”²

“. . . administering a blocking agent of VLA-4 antigens on the surface of hematopoietic stem cells and CD34⁺ cells causes **peripheralization** of these cells by mediating **release** of the cells from the **marrow** environment via disruption of interactions between VLA-4 and its microenvironmental ligands, such as fibronectin and/or VCAM-1 on stromal cells or in the ECM.”³

From the above, it is my understanding that Papayannopoulou *et al.*’s “peripheralization of hematopoietic stem cells” means “**increasing the number** of hematopoietic stem cells and CD34⁺ cells in peripheral blood”⁴ by **releasing** these cells from bone marrow into peripheral blood.

C. The claimed invention’s “adhesion” and Papayannopoulou *et al.* “periphalarization” are different

Based on the above-discussed teachings of the specification and prior art cited therein (item #5.A.), and on the disclosure of Papayannopoulou *et al.* (item #5.B.), it is my understanding that the claimed invention’s cell-to-cell “**adhesion**” is a **different phenomenon** from Papayannopoulou *et al.*’s “**peripheralization**.” In particular, the recited “adhesion” of HPCs refers to the **binding** of an extracellular domain of its integrin $\alpha 4 \beta 1$ membrane protein with a second molecule that is on the surface of another cell type, which is in contrast to Papayannopoulou *et al.*’s “peripheralization” of HPCs that means **releasing** these cells into the peripheral blood.

6. The claimed invention’s step c) was not necessarily included in the methods of Papayannopoulou *et al.*

Prior to the instantly claimed invention, the prior art was **ignorant** of a role of integrin $\alpha 4 \beta 1$ that is expressed on HPCs in the recited “**adhesion**” of these cells to “target tissue that is

² Papayannopoulou , page 6, lines 26-33.


³ (Emphasis added) Papayannopoulou , page 25, lines 1-9.

⁴ Papayannopoulou , page 6, lines 26-33.

not bone marrow endothelial tissue.” In view of this ignorance, it is my opinion that there is no scientific argument that would logically demonstrate that Papayannopoulou *et al.* actively carried out the recited step of “detecting” the level of a **hitherto unknown phenomenon**, *i.e.*, the recited phenomenon of “adhesion of said hematopoietic progenitor cells to said target tissue that is not bone marrow endothelial tissue.”

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: 12/07/2011

By: 
Dr. David Cheresch

CURRICULUM VITAE

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Personal: Date of Birth: May 6, 1953
Place of Birth: Detroit, MI

Positions Held:

2006-Present	Vice Chair for Research, Department of Pathology, UCSD, La Jolla, CA.
2005-Present	Professor, Department of Pathology, Moores UCSD Cancer Center, La Jolla, CA. Director for Translational Research, Moores UCSD Cancer Center
1996-2005	Professor, Department of Immunology, The Scripps Research Institute
1989-1996	Associate Professor, Department of Immunology, The Scripps Research Institute
1985-1989	Assistant Professor, Department of Immunology, The Scripps Research Institute
1984-1985	Senior Research Associate, Research Institute of Scripps Clinic
1982-1984	Postdoctoral Fellow, Research Institute of Scripps Clinic
1979-1982	Graduate Assistant Instructor, Dept. of Microbiology, University of Miami, Florida
1976-1978	Instructor, Microbiology, Florida International University, Miami, Florida

Education:

1982	Ph.D. Degree, Microbiology/Immunology, "A Mechanism of Immune Hyporesponsiveness in the Metastatic Breast Cancer Patient" University of Miami, Florida
1978	Masters Degree, Microbiology, "Characterization of a Non-productive Infection of HSV-2 in an SV-40 Transformed Hamster Cell" University of Miami, Florida
1975	B.S. Degree, Biology, University of Michigan, Ann Arbor, Michigan

Professional Societies:

- American Association for Cancer Research
- American Society for Cell Biology
- American Association for the Advancement of Science
- North American Vascular Biology Organization
- American Society for Hematology
- Metastasis Research Society

Honors/Awards and Administration:

2011	Organizer, Moores UCSD Cancer Center 7th Annual Translational Oncology Symp., La Jolla, CA External Scientific Advisory Board member, Program Project the at the University of California Irvine Keynote Lecture "Induction of the vascular pathological response". Angiogenesis Gordon Research Conference. Salve Regina University, Newport, RI.
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- Organizer, 23rd Usha Mahajani Symposium on Molecular Medicine, Salk Institute for Biological Studies, La Jolla, CA.
- Co-Organizer, 6th Annual Frontiers of Clinical Investigation Symposium “Vascular Disease 2011: Bench to Bedside”, La Jolla, CA
- Keynote address at the Yale’s Vascular Biology and Therapeutics Program retreat, West Haven, CT
- The Russell Ross Memorial Lecturer, American Heart Association Annual Meeting, Orlando, FL.
- 2010 Organizer, 22nd Usha Mahajani Symposium on Molecular Medicine, Salk Inst. La Jolla, CA.
- Keynote Lecture “MicroRNA-132 mediated loss of p120RasGAP activates quiescent endothelium to facilitate pathological angiogenesis”. 4th Mayo Clinic Angio Symposium. Mackinac Island, MI
- Invited External Advisory Board member, VIB Vesalius Research Center, Leuven, Belgium
- Organizer, Moores UCSD Cancer Center 6th Annual Translational Oncology Symp., La Jolla, CA
- Presidential Lecture, Weill Cornell Medical College, Ansari Stem Cell Institute, New York, NY
- Recipient, Paget-Ewing award from the Metastasis Research Society and the AACR
- 2009 Recipient, NIH MERIT award, CA50286
- Keynote Lecture “A Role for VEGF as a Negative Regulator of Pericyte Function and Blood Vessel Maturation”. Gordon Research Conference, Ventura, CA.
- Organizer, 20th Usha Mahajani Symposium, Salk Institute for Biological Studies, La Jolla, CA.
- 2008 Organizer, BIO Translational Research Forum “Maximizing the Relationship between Academia and the Private Sector, San Diego, CA
- Organizer, 4th Annual Translational Oncology Symposium, Moores UCSD Cancer Center, La Jolla, CA
- Organizer, 3rd Mayo Clinic Angiogenesis Symposium, Rochester, MN. “Targeting Angiogenesis Molecular Pathways”
- 2007 Organizer, Keystone Symposium "Host Cell Interaction and Response to the Cancer Cell", Keystone Resort, CO
- Keynote Lecture “Nanoparticle-mediated targeted drug delivery to the tumor vasculature”, Third Annual Meeting of the AANM, UCSD, La Jolla, CA
- Davis Distinguished Lecture “Integrins and Kinases in Neovascularization”, Cardiovascular Day 2007, University of Missouri, Columbia, MO
- Featured Speaker, “New Targets and Delivery Systems in Cancer Diagnosis and Treatment”, Sidney Kimmel Cancer Center, San Diego, CA.
- Highlight Lecture “Signaling Mechanisms in Angiogenesis”, Vasculata 2007. Chapel Hill, NC.
- 2006 Keynote Address, The Lurie Comprehensive Cancer Center, Northwestern University “Vascular Response to Growth Factors and the Extracellular Matrix”
- Elkin Distinguished Lecture, Emory University, Atlanta, GA. “The Role of Integrins in Regulating the Survival of Invasive Cells”
- 2005 Basic Science Lecture Award, American Society of Cytopathology 53rd Annual Scientific Meeting
- 2004 Visiting Professorship, University New Mexico Cancer Center, “Vascular Response to Ischemic Disease and Cancer”
- Cited by the ISI Essential Science Indicators as the fifth most-cited scientist in the field of angiogenesis research over this ten year period.
- 2003 Keynote Address, Cold Spring Harbor Laboratory “Vector Targeting Strategies for Therapeutic Gene Delivery”
- Keynote Address, The Medical University of South Carolina, Hollings Cancer Center Research Symposium, “Modulation of Angiogenesis & Apoptosis in Cancer Therapy”
- The Scripps Foundation for Medicine & Science and The Scripps Research Institute Lecture: Frontiers in Medicine, “Cancer Therapy: Targeted Destruction of Tumor Blood Vessels”
- 2002 Founder of TargeGen, Inc., San Diego, CA.
- Organizer, Keystone Symposium "Cell Biological Response to the Extracellular Matrix"
- Keynote Speaker, Society for Biological Therapy "Understanding Angiogenesis with Molecular Mechanisms"
- 2001 Fellow of the American Heart Association (F.A.H.A.)
- Organizer, Gordon Conference, "Angiogenesis"

- 2000 Chair, AACR Special Conferences in Cancer Research, "Angiogenesis & Cancer"
Organizer, Gordon Conference, "Vascular Cell Biology"
- 1999 Recipient, 75th Anniversary Spirit of Scripps Award
Co-Chair, Gordon Conference, "Angiogenesis and Microcirculation"
- 1998 Director of Scripps/Merck Joint Program on Angiogenesis
National Cancer Institute MERIT AWARD CA50286 - 1998-2006
Brooks, et al. Cell 85:1-20, 1996 chosen as most cited "Hot Paper" by The Scientist in the field of Cell Biology
Presidential Symposium Lecture, American Society of Hematology, Miami, Florida
7th Annual Dennis Woznicki Lecturer in Cardiovascular Pathology, Baylor College of Medicine, Houston, Texas
First Recipient of the Robert Bear Lectureship, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada
"Visiting Professor in Oncology," McGill University & The University of Montreal, Montreal, Quebec, Canada
Keynote address, Weinstein Cardiovascular Research Conference, Vanderbilt University, Nashville, TN
- 1997 Organizer, Keystone Symposium, "Angiogenesis & Vascular Remodeling" Steamboat Springs, CO
Myron Karon Memorial Lecturer, Children's Hospital at Los Angeles
XXIII Recipient of the Myron Karon Memorial Lectureship, University of Southern California, Los Angeles, California
15th Hans Lindner Memorial Lecture, Weizmann Institute of Science, Rehovot, Israel
Broadhurst Lecture, Schepens Institute, Harvard Medical School, Boston, MA
Deans Symposium Lecture, Medical College of Georgia, Augusta, GA
Member, Pathobiochemistry Study Section, NIH
- 1996 Robert Flynn Professorship Award, Lecture, Tufts University School of Medicine, Boston, MA, October 31, 1996
Organizer, Keystone Symposium: Integrins and Signaling Events in Cell Biology and Disease, Keystone, CO.
Donald and Darlene Shiley Lectureship, "Starving Tumors," La Jolla, CA
- 1992 Recipient of the American Cancer Society Faculty Research Award, 1992-1997.
- 1990 Cheresch et al. Cell 57:59, 1989 chosen as most cited "Hot Paper" by The Scientist in the field of Cell Biology
- 1988 "Distinguished Visitor" Anti-Cancer Foundation, Australia
- 1985 Recipient of the J. Ernest Ayre Memorial Junior Faculty Award given by the National Cancer Cytology Center

Editorial and Review Boards:

- 2010-Present Vascular Cell, Editorial Board Member
- 2006-2008 Volume Editor on "Integrins" and "Angiogenesis"
- 2002-2005 Cancer Biology & Therapy, Editorial Board Member
- 2001-2006 Alliance for Cancer Gene Therapy, Scientific Advisory Council
- 2001-2004 Hope Heart Institute, Scientific Advisory Board
- 2001-Present Vasculogenix, Scientific Advisory Council
- 2000-2003 Keystone Symposia, Scientific Advisory Board
- 1999-Present Endothelium, Journal of Endothelial Cell Research, Editorial Board
- 1999-Present Expert Reviews in Molecular Medicine, Editorial Board
- 1998-Present Molecular Medicine, Advisory Editorial Board
- 1998-2002 Circulation Research, Editorial Board Member
- 1997-Present Microvascular Research, Associate Editor
- 1997-Present Angiogenesis Research, Associate Editor
- 1997-Present Angiogenesis, Editorial Advisory Board
- 1997-Present Journal of Clinical Investigation, Board of Consulting Editors
- 1997-2001 NIH Pathobiochemistry Study Section
- 1996-Present Navbo Scientific Advisory Board Member
- 1995-1998 National American Heart Association Grant Reviewer

1992-Present Journal of Cell Science, Associate Editor
 1992-Present Cell Adhesion and Communication, Associate Editor
 1992 Volume Editor, "Receptors for the Extracellular Matrix" Biology of the Extracellular Matrix Academic Press.

Invited Lecturer:

- 2011** 1st Annual Collaborative Care Conference: "Targeting integrin $\alpha_v\beta_3$ in the treatment of glioblastoma multiforme", San Diego, CA
 Moores UCSD Cancer Center 7th Annual Symposium: "Targeting Raf by allosteric inhibition offers new therapeutic opportunities in oncology", La Jolla, CA
 AACR 2011 Annual Meeting: "microRNA regulation of the tumor angiogenic switch", Orlando, FL
 Oncology Research Seminar Series, Lilly Research Laboratories: "New insights into Raf as a target in oncology", Indianapolis, IN
 ASCO 2011 CME Satellite Symposium: Integrin Inhibitors in Glioblastoma & Solid Tumors: "The cilengitide story from discovery to the clinic and back", Chicago, IL
 Angiogenesis Gordon Research Conference, Salve Regina University: "Induction of the vascular pathological response"-Keynote Lecture, , Newport, RI
 Yale's Vascular Biology and Therapeutics Program Retreat: " α_v integrins and CRAF regulation of angiogenesis"-Keynote Lecture, West Haven, CT
 NAVBO workshop on Signaling in Cardiovascular Development: "MicroRNA-mediated regulation of the angiogenic switch", Cape Cod, MA
 AHA Annual Meeting: "Induction of the vascular pathological response"-The Russell Ross Memorial Lecture, Orlando, FL
- 2010** Research seminar in the Department of Pharmacology: "MicroRNA-132 mediated loss of p120Ras GAP activates quiescent endothelium to facilitate pathological angiogenesis", University of Illinois, Chicago, IL
 The Banbury Center, Cold Spring Harbor Laboratory Meeting: "MicroRNA-132 mediated loss of p120RasGAP activates quiescent endothelium to facilitate pathological angiogenesis", New York
 Frontiers in Cardiovascular Science Seminar Series: "MicroRNA-132 mediated loss of p120RasGAP activates quiescent endothelium to facilitate pathological angiogenesis", University of Michigan, Ann Arbor, MI
 16th Int'l Vascular Biology Meeting: "MicroRNA-132 mediated loss of p120RasGAP activates quiescent endothelium to facilitate pathological angiogenesis", UCSL, Los Angeles, CA
 Gordon Research Conference: "Vascular growth factor biology in the context of therapy", University of New England, Biddeford, ME
 The 16th Meeting on Protein Phosphorylation and Cell Signaling: "Allosteric Inhibitors of Raf Suppress Tumor Growth by Preventing Raf Dimerization", Salk Research Institute, La Jolla, CA
 Research seminar, Department of Oncological Sciences: "Unexpected role of Raf in tumor cell mitosis revealed by an allosteric inhibitor", Mount Sinai SOM, New York, NY
 Distinguished Seminar Series, Herbert Irving Comprehensive Cancer Center: "Unexpected role of Raf in tumor cell mitosis revealed by an allosteric inhibitor", Columbia University, New York, NY
- 2009** Keystone symposium: "A Role for VEGF as a Negative Regulator of Pericyte Function and Blood Vessel Maturation", Big Sky, MT
 2009 ASCO-Gastrointestinal Cancer Symposium: "A Role for VEGF as a Negative Regulator of Pericyte Function and Blood Vessel Maturation", San Francisco, CA
 University of California Irvine Scientific Seminar Series: "Unexpected role of VEGF in the tumor microenvironment: New insights into cancer therapy", Irvine, CA
 AACR 100th Annual Meeting: "A Role for VEGF as a Negative Regulator of Pericyte Function and Vessel Maturation: Important Implications for Cancer Therapy", Denver, CO
 Int'l Conference of the American Thoracic Society: "Endothelial cell survival signals from the tumor microenvironment", San Diego, CA

- Gordon Research Conference on Angiogenesis: "VEGF actions on pericyte function", Salve Regina University, Newport, RI.
- The 2nd Int'l Kloster Seeon Meeting: "miR-132 acts as an angiogenic switch by suppressing endothelial 120RasGAP", Kloster Seeon, Germany
- The 4th Annual NCI Alliance for nanotechnology in Cancer Investigators' Meeting: "Neovascular Targeted Lipid-Coated Nanogels as Versatile Drug Carriers", Manhattan Beach, CA
- 2008** Keystone symposium: "Disruption of B-RAF/C-RAF Dimerization Blocks, Angiogenesis and Tumor Growth", Vancouver, CA
- 10th Int'l Symposium on Anti-angiogenic Agents: "A Chemical/Biology Approach to Develop New Anti-angiogenic Agents", La Jolla, CA
- International workshop: "Developing a New Class of Tyrosine Kinase Inhibitors to Target Cancer and Angiogenesis", Kyoto, Japan
- The UCSD Hematology/Oncology Conference "Targeting Rf in the Tumor Vasculature", La Jolla, CA
- Keystone symposium: "Raf Kinase as Target for Tumor Growth and Angiogenesis", Snowbird, UT
- ESH 8th Int'l Euroconference on Angiogenesis: "Targeting Raf in the tumor endothelium", Paris, FR
- Salk Research Institute Mini-Symposium on Targeted Therapeutics in Cancer: "New Strategy for Targeting Kinases in Tumors and Neovasculature", La Jolla, CA
- NAVBO Workshop: "Role of Raf in Vascular Development and Angiogenesis", Cape Cod, MA
- The Cell & Molecular Physiology Series Seminar: "A Role for VEGF as a Negative Regulator of Pericyte Function and Blood Vessel Maturation" University of North Carolina, Chapel Hill, NC
- 3rd Mayo Clinic Angiogenesis Symp: "Targeting Angiogenesis Molecular Pathways", Rochester, MN
- iSBT Annual Meeting: "Anti-angiogenic Therapies", San Diego, CA
- 2007** Roswell Park Cancer Institute: "Targeting the Tumor Blood Vessels", Buffalo, NY
- Duke University: "Targeting Raf Kinase in the Angiogenic Endothelium", Durham, NC
- AACR 98th Annual Mtg: "Metastasis Regulation by Caspase/Integrin Cooperation", Los Angeles, CA
- 2nd International Symposium on Cancer Metastasis and the Lymphovascular System: "Role of the Tumor Microenvironment on Tumor Cell Survival and Metastasis", San Francisco, CA
- 2007 NSTI/NCI Symposium: "Nanotechnology for Cancer Prevention, Diagnosis and Treatment", Santa Clara, CA
- University of Michigan School of Medicine, "Molecular Signals in Angiogenesis", Ann Arbor, MI
- Van Andel Research Inst: "Signaling Mechanism in Angiogenesis and Metastasis", Grand Rapids, MI
- Univ of Texas MD Anderson Cancer Ctr: "Molecular Targets in Tumor Angiogenesis", Houston, TX
- 6th Annual Int'l Congress on the Future of Breast Cancer: "Attacking the Metastatic Cascade", Kohala Coast, HI
- Keystone Symp: "Integrin Roles in Tumor Angiogenesis and Lymphangiogenesis", Keystone, CO
- UCSD Physiology Seminar: "Signaling Pathways in Angiogenesis: Role of Raf Kinase in the Patterning of New Blood Vessels", San Diego, CA
- 2007 IRACDA National Conference: "Entrepreneurial Science", San Diego, CA
- RAI Seminar Series: "Signaling Mechanisms in Angiogenesis", La Jolla, CA
- University of Chicago Biomedical Sciences Cluster Seminar Series: "Raf Kinase in Endothelial Cell Survival and Angiogenesis", Chicago, IL
- Burnham Institute for Medical Research Cancer Center Series. "A Chemical/Biology Approach to Develop New Anti-angiogenic Agents", La Jolla, CA
- 2006** 8th International Symposium on Anti-Angiogenic Agents, La Jolla, CA, "Vascular Signaling Mechanisms in the Tumor Endothelium"
- Scientific Writers Conference, Moores UCSD Cancer Center, La Jolla, CA, "Angiogenesis: Is blocking the Flow of Blood to Tumors a Good Way to Fight Cancer?"
- Angiogenesis Research & Therapeutics Conference, Old Town, San Diego, CA, "Selective Blockade of the Permeability-Inducing Effects of VEGF during Ischemic Disease and Macular Edema"
- WCSDB 2006 Regional Meeting, Asilomar Conference Center, Pacific Grove, CA.
- University of Utah Medical Seminar Series, Salt Lake City, "Therapeutic Targeting of the Tumor Vasculature"
- AACR 97th Annual Meeting, Washington, DC, "Therapeutic Implications of Integrin-Mediated Signals in the Tumor Vascular Compartment"

NHLBI US-INSERM Symposium on Angiogenesis, Cellular & Gene Therapy, Denver, CO, "Role of VEGF and the Vascular Barrier Function in Disease"

Society for Nuclear Medicine Categorical Seminar, San Diego, CA, "Molecular Basis of Angiogenesis"

Keynote Address, Angiogenesis Symposium, The Lurie Comprehensive Cancer Center, Northwestern University "Vascular Response to Growth Factors and the Extracellular Matrix"

Elkin Distinguished Lecture, Emory University, "Cell Survival, a Critical Determinant in Metastatic Disease and Angiogenesis"

5th International Congress on Targeted Therapies in Oncology, "Targeting Integrins"

18th Annual Usha Mahajani Symposium, Salk Institute, "Regulation of Metastatic Disease by Cell Adhesion Receptor Signaling"

Plenary Speaker, International Society for Oncodevelopmental Biology and Medicine, Pasadena, CA., "Vascular Response to Growth Factors and the Extracellular Matrix"

UCSF Biomedical Seminar Series, San Francisco, CA., "Cell Survival, a Critical Determinant in Metastatic Disease and Angiogenesis"

National Cancer Institute, Nanotechnology Alliance Investigators Meeting, San Diego, CA., "Targeting nanoparticles to the Tumor Endothelium"

Academic Pathology Chairs & Administrator's Meeting, Coronado, CA., "Translational Research in Pathology"

Mayo Clinic Angiogenesis Symposium, Rochester, MN., "Role of Raf Kinase in Endothelial Cell Survival and Angiogenesis"

National Cancer Institute Board of Scientific Advisors, Bethesda, MD., "Selective Ablation of Metastatic Disease by Nanoparticle-targeted Drug Delivery to the Neovasculature"

Fine Particle Society 2006 International Conference on Bio and Pharmaceutical Science and Technology, San Diego, CA., "Nanoparticle-mediated Drug Delivery to the Tumor vasculature Disrupts Metastatic Disease"

2005 Cell Migration & Adhesion Symposium, University of North Carolina at Chapel Hill, "Disease Implications of Integrin Regulation of Angiogenesis"

Gordon Research Conference, Ventura, CA, "Physiological Consequences of Vascular Cell Adhesion Mechanisms"

Miami Nature Biotechnology Winter Symposium University of Miami, "Growth Factor Signaling in the Tumor Endothelium"

7th International Symposium on Anti-Angiogenic Agents, Hyatt Regency La Jolla, "Unexpected Role of VEGF in Ischemic Disease and Cancer"

Sidney Kimmel Cancer Center Gene Therapy Conference, Hotel Del Coronado, "Targeting Vascular Cell Signaling Pathways in Tumors"

UC Davis Cancer Research Seminar Series, Sacramento, **CA. "Vascular Events in Cancer & Ischemic Disease"**

13th International AEK/AIO Cancer Congress of the German Cancer Society, Wurzburg, Germany, "Unexpected Role of VEGF in Tumor Cell Invasion & Metastasis"

Keystone Symposium, Steamboat Springs, Colorado, "Integrins in Cell Invasion & Migration"

American Thoracic Society, San Diego, "Apoptotic Cues from the ECM: Regulators of Angiogenesis"

Gordon Research Conference, Newport, Rhode Island, "Vascular Response to Growth Factors and the Extracellular Environment"

Moore's UCSD Cancer Center La Jolla, CA, "Anti-Angiogenesis: Attacking the Cancer Blood Supply"

Translational Research Conference, La Jolla, CA, "Therapeutic Targeting of the Tumor Vascular Compartment"

Molecular Pathology Graduate Program, La Jolla, CA, "Integrin Signaling in Health and Disease"

Loyola University Medical Center, Chicago, IL, "Vascular Response to Ischemic Disease and Cancer"

Borrego Springs Retreat, Borrego Springs, CA, "Tumor Microenvironment & Metastasis"

Molecular Biology Program, La Jolla, CA, "Integrin Signaling in Health and Disease"

1st Moore's UCSD Cancer Center Symposium, La Jolla, CA, "New Targets in Oncology"

CME for Physicians, Moore's UCSD Cancer Center, "Targeting the Tumor Vasculature for Imaging and Treatment of Cancer"

Molecular Pharmacology & Chemistry Seminar Series, Sloan-Kettering Institute, "VEGF Activation of Blood Vessels and its Pathophysiological Consequences"

1st Annual Mellon Institute Symposium, University of Virginia, Charlottesville, VA, "Targeting Endothelial Cell Signaling Pathways in Disease"

11th Annual Penn State Cancer Center Symposium, Hershey, PA, "Growth Factor & Extracellular Matrix Signals Regulating Tumor Angiogenesis and Metastasis"

TargeGen Scientific Advisory, La Jolla, CA, "Recent Developments in the Pathophysiological Effects of VEGF-Induced Vascular Permeability"

53rd American Society of Cytopathology, San Diego, CA, "Vascular Response to Ischemic Disease and Cancer"

AACR Special Conference in Cancer Research, Boston, MA, "Unexpected Role of VEGF in Tumor Cell Invasion and Metastasis"

Yale University 2005/2006 Seminars, New Haven, CT, "Regulation of Tumor Angiogenesis and Metastasis by Growth Factor and Extracellular Matrix Signals"

2004 Dartmouth Life Sciences Symposium, Unexpected Role of VEGF in Ischemic Disease & Cancer, Hanover, NH

Memorial Sloan-Kettering Cancer Center, Biological Consequences of Signaling in the Vascular Compartment, New York, NY

Biofunding Summit, Limiting Ischemic Damage Through Control of Vascular Permeability, LaJolla, CA

Genentech Seminar Series, Unexpected Role of VEGF in Cardiovascular Disease & Cancer, S. San Francisco, CA

Keynote Speaker, DOBI Medical International, What is going on in Cancer/Angiogenesis Research, Mahwah, New Jersey

International Congress of Histochemistry & Cytochemistry, Signaling Pathways in Tumor Angiogenesis & Metastatic Disease, LaJolla, CA

Gordon Research Conference, Signal Transduction by Engineered Extracellular Matrices, Lewiston, ME

Trans-Institute Angiogenesis Workshop, Towson, Maryland

Memorial Sloan-Kettering Cancer Center, Signaling Events in Vascular Remodeling & Angiogenesis, New York, NY

Fifth Annual Conference, Arteriosclerosis, Thrombosis & Vascular Biology, San Francisco, CA

Experimental Biology Symposium, Biological Applications of Nanotechnology, Washington, DC

Rockefeller University, Unexpected Role of VEGF in Cardiovascular Disease & Cancer, New York, NY

The Burnham Institute, Signalling Events in Vascular Remodeling & Angiogenesis, LaJolla, CA

Sixth International Symposium on Anti-Angiogenic Agents, LaJolla, CA.

Keystone Symposium, Angiogenesis- Novel Basic Science Insights and Human Therapy, Santa Fe, NM

2003 UNM CRTC Visiting Professorship, Signalling Events in Vascular Remodeling and Angiogenesis

American Society of Hematology, 45th Annual Meeting, San Diego, CA.

Fourth International Conference on Systems Biology, Washington University, St. Louis, MO.

Chiron Corporation, "Targeted Molecular Therapy for Vascular Disease", San Francisco, CA.

American Association for Cancer Research, "Advances in Breast Cancer Research: Genetics, Biology & Clinical Implications", Huntington Beach, CA.

University of Miami, "Role of the Endothelial Cell Src Kinase in Myocardial Infarction", Miami, FL.

Fifteenth Annual Mahajani Symposium, "Animal Models & Imaging: Recent Advances in Cancer Research, La Jolla, CA.

GTCBIO Conference, "Cardiovascular Drug Discovery & Development", San Diego, CA.

Norris Comprehensive Cancer Center, "Therapeutic Targeting of the Tumor Vasculature", Los Angeles, CA

Gordon Research Conference, Angiogenesis & Microcirculation, Newport, RI.

American Association for Cancer Research, 94th Annual Meeting, Washington, D.C.

Gordon Research Conference, Atherosclerosis, Meriden, New Hampshire

American Heart Association, Arteriosclerosis, Thrombosis, and Vascular Biology, Washington, D.C.

Duke University Medical Center, Brain Tumor Seminar Series, Durham, North Carolina

The University of North Carolina, Seminar Series, Chapel Hill, NC.

- Experimental Biology/NAVBO/ASIP Annual Meeting, San Diego, CA.
The Scripps Foundation for Medicine & Science and The Scripps Research Institute Lecture: Frontiers in Medicine, "Cancer Therapy: Targeted Destruction of Tumor Blood Vessels"
Cold Spring Harbor Laboratories, "Vector Targeting Strategies for Therapeutic Gene Delivery"
The University of Texas MD Anderson Cancer Center, 44th Annual Clinical Conference: Molecular Therapeutics for Cancer Metastasis, Houston, TX.
University of California at San Diego, Cancer Center Lecture Series, San Diego, CA.
The Scripps Cancer Center Scientific Retreat, "Therapeutic Targeting of Tumor Blood Cells"
The Medical University of South Carolina, Hollings Cancer Center Research Symposium, "Modulation of Angiogenesis & Apoptosis in Cancer Therapy", Charleston, NC.
University of Miami School of Medicine, Seminar Program, Miami, FL.
The Children's Hospital, Symposium in Honor of Dr. Judah Folkman, Boston, MA.
University of California at Los Angeles, Vascular Biology Seminar Series, Los Angeles, CA.
Keystone Symposium, Molecular Mechanisms of Apoptosis (B6), Banff, Canada
The Center for Biomedical Continuing Education, 5th International Symposium on Anti-Angiogenic Agents, La Jolla, CA
Gordon Research Conference, Vascular Cell Biology, Ventura, CA.
The Center for Biomedical Continuing Education, 3rd Annual Opinion Leader Summit: "Targeted Therapies for the Treatment of Lung Cancer", Aspen, CO.
- 2002** Sidney Kimmel Cancer Center, 11th International Conference on Gene Therapy, San Diego, CA
The Knowledge Foundation, Gene Delivery – Non-viral Systems & in vivo Applications, San Diego, CA
The American Society for Cell Biology, 42nd Annual Meeting, San Francisco, CA
University of California San Diego, Cardiovascular Science Conference, San Diego, CA
The Center for Biomedical Continuing Education, 4th International Symposium on Anti-Angiogenic Agents, Dallas, TX
Keystone Symposia on Biological Response to the Extracellular Matrix, Banff, Canada
Keystone Symposia on Protein Phosphorylation & Mechanisms of Cellular Regulation, Taos, NM
St. Jude Children's Hospital, Education Program, Memphis, TN
Cold Spring Harbor Laboratories, 67th Symposium on Quantitative Biology "The Cardiovascular System", Cold Spring Harbor, NY
University of Texas, Pharmacology Seminar Series, Dallas, TX
Gordon Research Conference, Signaling by Adhesion Receptors, New London, CT
Breast Cancer International Research Group, 3rd International Conference, Anaheim, CA
The Center for Biomedical Continuing Education, 1st Annual Symposium on Anti-Receptor Signaling in Human Neoplasia, Chicago, IL
Society for Biological Therapy, Angiogenesis Workshop, San Diego, CA
American Society for Matrix Biology Conference, Houston, TX
American Society for Cell Biology Symposium Lecture, 42nd Annual Mtg., San Francisco, CA
- 2001** Gordon Research Conference, Fibronectin, Integrins and Related Molecules, Ventura, CA
Keystone Symposium, Cell Migration and Invasion, Tahoe City, CA
Stanford University School of Medicine, Stanford, CA
SUNY Stony Brook, School of Medicine, Scholars in Cancer Research, Stony Brook, NY
University of Wisconsin, Frontiers in Pharmacology, Madison, WI
Keystone Symposia on Molecular & Cellular Biology, Keystone, CO
- 2000** Keystone Symposia on Molecular & Cellular Biology, Joint Regulation of Signaling Pathways by Integrins & Growth Factors, Breckenridge, CO
Gordon Research Conference, Signaling by Adhesion Receptors, Newport, RI
Chair, Gordon Research Conference, Vascular Cell Biology, Plymouth, NH
Keystone Symposia on The Dynamics of the Cytoskeleton/Intercellular Junctions, Keystone, CO.
Biomedical Sciences Seminar Series, UCSF, San Francisco, CA
Keystone Symposia on Experimental & Clinical Regulation of Angiogenesis, Salt Lake City, Utah
Experimental Biology Meeting (FASEB), Signal Transduction & Angiogenesis, San Diego, CA
John Wayne Cancer Institute Seminar, Santa Monica, CA
UCSD/Salk Institute Mahajani Symposium, La Jolla CA
Georgetown University Medical Center, Oncology Grand Rounds, Washington, D.C.
AACR Special Conference on Angiogenesis, Traverse City, MI
Angiogenesis Seminar, The Wistar Institute, Philadelphia, PA

American Heart Association, Council on Arteriosclerosis, Thrombosis and Vascular Biology, New Orleans, LA

- 1999 UIC, Gynecologic Oncology Group Symposium, Nashville, TN
1st International Symposium on Anti-Angiogenic Agents, Irving, TX
The Gynecological Oncology Research Group Lecture Series, Boston, MA
Beth Israel Deaconess Medical Center, Boston, MA
IBC's 5th Annual Conference on Angiogenesis, Boston, MA
Keynote Speaker, Robert Wood Johnson Medical School, 1st Annual Research Day, New Brunswick, NJ
Vascular Biology, Matrix Remodeling in Angiogenesis, Washington, DC
University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC
Gordon Research Conference, Molecular Cell Biology, Tilton, NH
ISHR, Cardiovascular Research in the new Millennium - XXI Century, XXI Annual Scientific Sessions, San Diego, CA
National Cancer Institute, Third National AIDS Malignancy Conference, Bethesda, MD
Gordon Research Conference, Cell Contact and Adhesion, Proctor Academy, NH
Gordon Research Conference, Angiogenesis & Microcirculation, Salve Regina University, Newport, RI
Georgetown University Medical Center, Oncology Grand Rounds, Washington, DC
Ludwig Institute for Cancer Research, Salk Institute, Cancer on the Eve of the Millennium: Diagnostics, Therapy & Prevention, San Diego, CA
AACR Special Conference, Molecular Aspects of Metastasis, Snowmass, CO
Horizons in Vascular Biology & Therapeutics, Miami, FL
1998 Keystone Symposia Conference, Wound Repair, Copper Mountain, CO
AACR Special Conference, Angiogenesis and Cancer, Orlando, FL
Keystone Symposia Conference, Motility and Metastasis, Copper Mountain, CO
Keystone Symposia Conference, Endothelium, Lake Tahoe, NV
Keystone Symposia Conference, Molecular Biology of the Cardiovascular System, Steamboat Springs, CO
Keystone Symposia Conference, Angiogenesis and Vascular Remodeling, Steamboat Springs, CO
2nd International Symposium, Science and Medicine, Vascular Protection: From Basic Science to the Clinic, Los Angeles, CA
BACR/IACR Joint Annual Scientific Meeting, Dublin, Ireland
Brazilian Symposium on Extracellular Matrix, Rio de Janeiro, Brazil
VII International Congress of the Metastasis Research Society, San Diego, CA
1st Annual Robert Bear Lectureship, Toronto, Ontario, Canada
Schering Foundation Workshop, Therapeutic Angiogenesis: From Basic Science to the Clinic, San Francisco, CA
Annual Meeting of the American Society of Hematology, Miami Beach, FL
Science & Medicine Second International Symposium, Vascular Protection: From Basic Science to the Clinic, Los Angeles, CA

Patents:

- 7.833.976 Methods for treatment of tumors and metastases using a combination of anti-angiogenic and immune therapies. 11/16/2010
7.803.399 Delivery system for nucleic acids. 09/28/2010
7.595.051 Methods of treating neovascular glaucoma, macular degeneration and capillary proliferation with alphavbeta3-specific antibodies. 09/29/2009
7.585.841 Methods and compositions useful for modulation of angiogenesis using tyrosine kinase Src. 09/08/2009
7.482.007 Methods for inhibiting angiogenesis to treat cancer with alphavbeta3-specific antibodies. 01/27/2009
7.368.478 Methods for inhibiting angiogenesis and tumor growth. 05/06/2008
7.365.054 Methods for treatment of tumors and metastases using a combination of anti-angiogenic and immune therapies. 04/29/2008

- 7.354.586 Methods of treating arthritis and diabetic retinopathy with .alpha sub.v.beta sub.3-specific antibodies. 04/08/2008
- 7.329.406 Methods of treating psoriasis with .alpha sub.v.beta sub.3-specific antibodies. 02/12/2008
- 7.125.849 Peptide-based angiogenesis inhibitors and methods of use thereof. 10/24/2006
- 7.115.660 Methods for inhibiting angiogenesis and tumor growth. 10/03/2006
- 7.115.261 Methods for treatment of tumors and metastases using a combination of anti-angiogenic and immune therapies. 10/03/2006
- 7.053.041 Methods and compositions useful for inhibition of .alpha..sub.v.beta..sub.5mediated angiogenesis. 05/03/2006
- 7.025987 Delivery system for nucleic acids. 04/11/2006
- 6.887.473 Inhibition of angiogenesis in disease states with an anti-alpha.v.beta.3 monoclonal antibody. 05/03/2005
- 6.803.383 Inhibition of angiogenesis and tumor growth. 10/12/2004
- 6.685.938 Methods and compositions useful for modulation of angiogenesis and vascular permeability using SRC or Yes tyrosine kinases. 02/03/2004
- 6.500.924 Methods and compositions useful for inhibition of angiogenesis. 12/31/2002
- 5.866.540 Cyclic adhesion inhibitors. 02/02/1999
- 5.766.591 Methods and compositions useful for inhibition of angiogenesis. 06/16/1998
- 5.753.230 Methods and compositions useful for inhibition of angiogenesis. 05/19/1998

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